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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/810,277      | 03/26/2004  | Frits Goedegebuur    | GC794-2             | 8580             |

5100 7590 01/08/2007  
GENENCOR INTERNATIONAL, INC.  
ATTENTION: LEGAL DEPARTMENT  
925 PAGE MILL ROAD  
PALO ALTO, CA 94304

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| EXAMINER |
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CHOWDHURY, IQBAL HOSSAIN

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1652

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE  | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS                               | 01/08/2007 | PAPER         |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

|                              |                           |                     |  |
|------------------------------|---------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b>    | <b>Applicant(s)</b> |  |
|                              | 10/810,277                | GOEDEGEBUUR ET AL.  |  |
|                              | <b>Examiner</b>           | <b>Art Unit</b>     |  |
|                              | Iqbal H. Chowdhury, Ph.D. | 1652                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 2,5-16,18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-4 and 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/05</u> .   | 6) <input type="checkbox"/> Other: _____                          |

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### DETAILED ACTION

Claims 1-19 are pending.

Applicant's election with traverse of Group I, Claims 1-5 and 17, drawn to an isolated variant polypeptide having cellobiohydrolases 1 activity and variant protein of SEQ ID No: 4 or a nucleic acid encoding SEQ ID No: 4 in the response filed on 11/3/2006 is acknowledged.

The traversal is on the ground(s) that there would be no burden of search for the coexamination of all the groups I-III simultaneously, specifically Group I and II, which are directed to polypeptide (Group I) and polynucleotide (Group II). This is not found persuasive because while the search necessary for examination of all the groups overlaps, it is not coextensive, examination of Group II-III would require search of subclasses unnecessary for the search of Group I, for example 435/209, 435/252.3 and 209 and 435/99. Besides, the DNA of Group II and the protein of Group I each comprise a chemically unrelated structure capable of separate manufacture, use and effect. The DNA comprises a nucleic acid sequence of group II and the protein of Group I comprises amino acid sequences. The DNA has other utility besides encoding the proteins such hybridization or probe preparation and the proteins can be made by another method such as isolation from natural sources or chemical synthesis. Thus, examining all the groups would create a serious search burden to the Examiner. As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

Applicants further argue to search nucleic acid and amino acid sequence of Subgroup (A)-(I) i.e. nine sequences. This is not persuasive because contrary to applicants arguments, a search for each of the sequences would not be done solely by searching electronic sequence

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databases as such databases seldom provide extensive coverage of all variants which are known or have been made of a single protein such that word searching for each variant is required. Such searching would likely be different for each variant as each change may have distinct effects. Furthermore, even sequence searching of the nine different sequences would be a substantial search burden on the Examiner, as each sequence has to be examined individually to determine if it includes variant. As such the novelty and non-obviousness of each variant would have to be addressed individually creating a large search burden on the office. However, the Examiner has agreed to examine SEQ ID NO: 3 and 4 in view of applicants persuasive arguments that SEQ ID NO: 4 is the same sequence as residues 19-525 of SEQ ID NO: 3 contains the signal sequence while SEQ ID NO: 4 does not.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 2, 5-16 and 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 3-4 and 17 are under consideration and are being examined herein.

#### ***Priority***

Acknowledgement is made of applicants claim for priority of provisional application 60/459,734 filed on 04/01/2003.

#### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on 9/19/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the Examiner.

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### ***Drawings***

The Examiner objected to the drawings of this application due to the presence of nucleic acid and protein sequence without sequence identifier i.e. SEQ ID NOs submitted on 3/26/2004. Therefore, drawings are not considered by the examiner. See particularly 37 CFR 1.821(d).

### ***Claim Objections***

Claim 1 is objected to as encompassing non-elected subject matter. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 101***

In the absence of the hand of man, naturally occurring nucleic acids and /or proteins are considered non-statutory subject matter. *Diamond and Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified polypeptide". For examination purpose the claim is read as such.

Claims 1 and 3-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 3-4 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present instance, claim 1 recites "CBH1.1

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variant” which is unclear as to the scope of mutants of CBH that are encompassed. In another words, how many changes can be made to a CBH enzyme and still be a “CBH1.1 variant”?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide having cellobiohydrolases I (CBH) activity of SEQ ID NO: 3 (plus signal sequence) and SEQ ID NO: 4 from *Humicola grisea*, does not reasonably provide enablement for any variant having CBH activity and having no known identity to SEQ ID NO: 3 and 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-4 and 17 are so broad as to encompass any variants of SEQ ID NO: 3 and 4 having CBH activity or a composition comprising any variants of SEQ ID NO: 3 and 4 having CBH activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants of SEQ ID NO: 3 and 4 broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in

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which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single variant protein having CBH activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all variants of SEQ ID NO: 3 and 4 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting CBH activity and; (B) the general tolerance of CBH protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any variants residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any variant of SEQ ID NO: 3 and 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any variant of SEQ ID NO: 3 and

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4 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-4 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Takashima et al. (UniProt Accession No. Q12621, created 11/1/1996, "Cloning, sequencing, and expression of the cellulase genes of *Humicola grisea* var. *thermoidea*"). Instant claims drawn to variant polypeptide and a composition comprising said variant polypeptide having cellobiohydrolase i.e. converting cellulose to glucose, activity isolated from *Humicola grisea* var. *thermoidea*.

Takashima et al. teach a cellulase (converts cellulose to glucose) gene encoding protein, which is 99.8% identical to SEQ ID NO: 3 and 4 of the instant application, inherently a cellobiohydrolase, isolated from the same source *Humicola grisea* var. *thermoidea* as the applicants (claims 1 and 3-4). Since variants do not have any limitation in the extent of modification. Therefore, a polypeptide, which is 99.8% to SEQ ID NO: 3 or 4, reads on a variant of SEQ ID NO: 3 or 4 of the instant application. Claim 17 is also included in this rejection because a composition comprising said variant polypeptide is nothing but the recited polypeptide

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of Takashima et al. Therefore, Takashima et al. anticipate claims 1, 3-4 and 17 of the instant application.

Claims 1, 3-4 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Lange et al. (WO2003000941, publication 1/3/2003, filed on 6/26/2002, "New polypeptide with cellobiohydrolase I activity, useful in producing ethanol from biomass). Instant claims drawn to variant polypeptide and a composition comprising said variant polypeptide having cellobiohydrolase i.e. converting cellulose to glucose, activity isolated from *Humicola grisea* var. *thermoidea*.

Lange et al. teach a cellobiohydrolase isolated from *Humicola* sp, which is 99.8% identical to SEQ ID NO: 3 and 99.6% identical to SEQ ID NO: 4 of the instant application and method of use of said polypeptide. Since variants do not have any limitation in the extent of modification. Therefore, a polypeptide, which is 99.8% to SEQ ID NO: 3 or 99.6% identical to SEQ ID NO: 4, reads on a variant of SEQ ID NO: 3 or 4 of the instant application (claim 1 and 3-4). Claim 17 is also included in this rejection because a composition comprising said variant polypeptide is nothing but the recited polypeptide of Lange et al. Therefore, Lange et al. anticipate claims 1, 3-4 and 17 of the instant application.

### ***Conclusion***

#### **Status of the claims:**

Claims 1-19 are pending.

Claims 1, 3-4 and 17 are rejected.

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No claim is in condition for allowance.

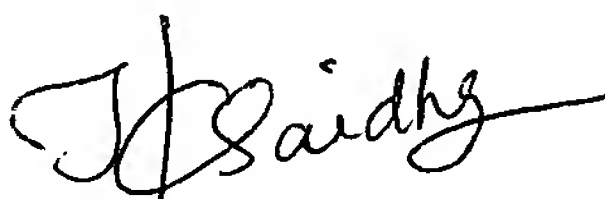
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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